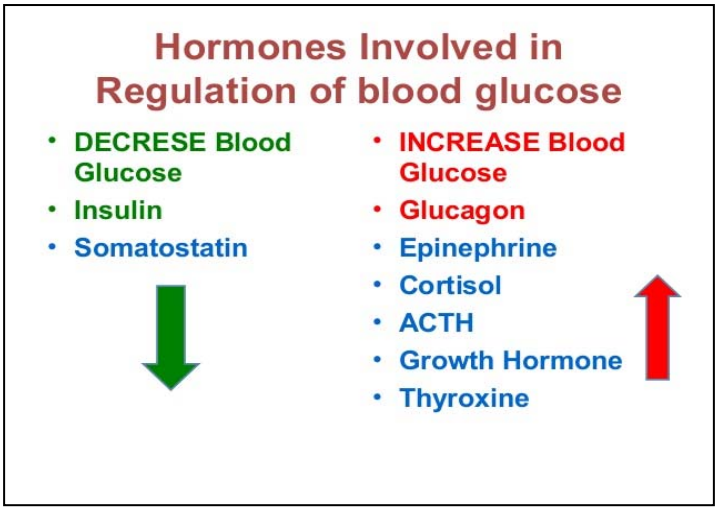
Diabetes Mellitus

Diabetes mellitus is not one disease, but rather is a heterogeneous group of multifactorial, polygenic syndromes characterized by an elevation of fasting blood glucose caused by a relative or absolute deficiency in insulin. It leads to disturbance in carbohydrate, lipid, protein and mineral metabolism.

- **Blood glucose levels are controlled by a complex interaction of multiple chemicals and hormones in the body, including the insulin hormone made in the beta cells of the pancreas.**

- **Insulin insufficiency leads to reduction in tissue uptake of glucose which cause:**
  - **Intracellular hypoglycemia**
  - **Extracellular hyperglycemia**

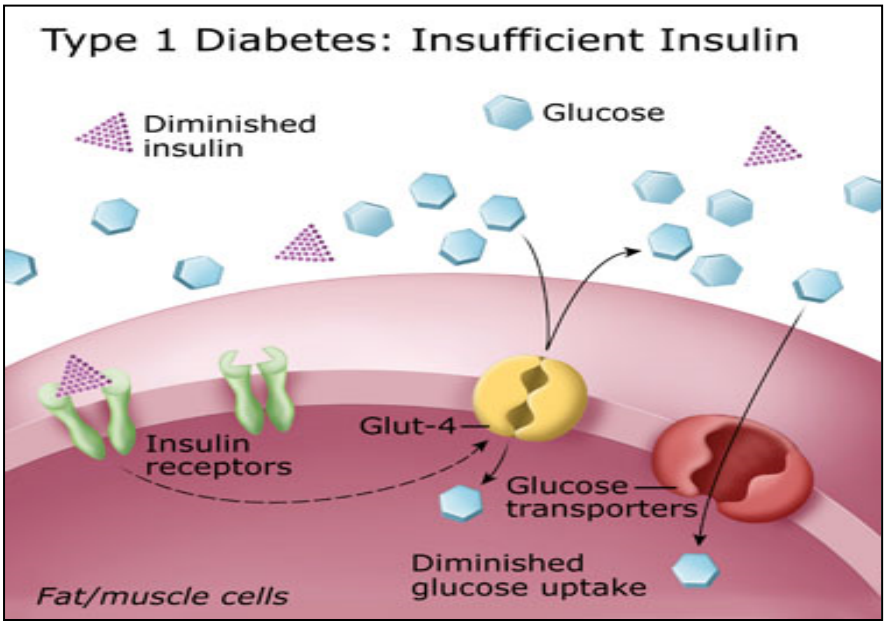


General Signs and Symptoms of DM:

1- Polyuria.
2- Polydypsea.
3- Polyphagia.
4- Loss of weight.
5- Dehydration.
6- Glucosuria.

Type I Diabetes

- ✓ It constitutes about **10%** of diabetics.
- ✓ Characterized by **absolute deficiency of insulin** caused by an autoimmune attack on β cells of the pancreas
- ✓ Symptoms appear suddenly when **80-90%** of the cells are destroyed.



Metabolic changes in Type 1 diabetes:

1-Carbohydrates metabolism:

The hallmarks of diabetes mellitus is Hyperglycemia which is caused by:

- Decrease Glucose uptake by GLUT4 which mainly affect muscle and adipose tissues
- Increased hepatic production of glucose (glycogenolysis and gluconeogenesis)

2- Lipid metabolism (Hypertriacylglycerolemia)

a) Increase of lipolysis leads to release of fatty acids

b) -These excess fatty acids are converted to triacylglycerol, which is packaged and secreted in very-low-density lipoproteins (VLDL)…
-Because lipoprotein degradation catalyzed by lipoprotein lipase in the capillary beds of muscle and adipose tissue is low in diabetics (synthesis of the enzyme is decreased when insulin levels are low)
-SO the plasma chylomicron and VLDL levels are elevated, resulting in hypertriacylglycerolemia

All these may lead to atherosclerosis

c) Ketoacidosis (Ketosis): results from increased mobilization of fatty acids from adipose tissue, combined with accelerated hepatic fatty acid β-oxidation and synthesis of ketone bodies.

3. Protein metabolism

a) Increased protein breakdown to be used in gluconeogenesis
b) Decrease antibody formation which leads to recurrent infections.

Complications of type I Diabetes:

1- **Diabetic Ketoacidosis**: 25-40 %

- *Clinically:*

- Coma
- Dry skin
- Hyperventilation
- Acetone odour in mouth

- *LAB Data:*

- High blood glucose
- Glucose and acetone in urine
- Increase K in blood

2- Hypoglycemic coma: due to insulin overshoot

- *Clinically:*

- Coma
- Moist skin
- No hyperventilation
- No acetone odour in mouth.

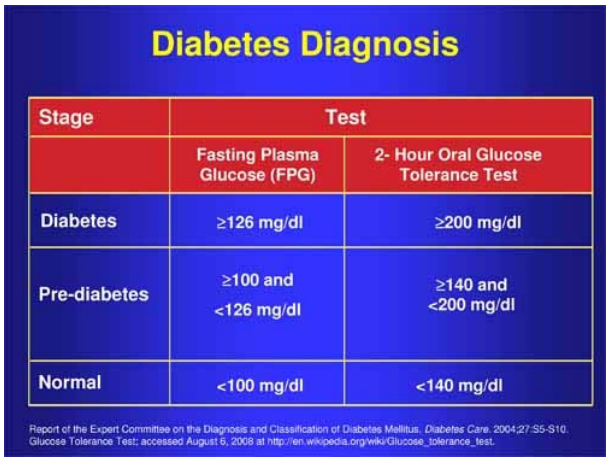
- *Lab data:*

- Low blood glucose.
- No glucose or acetone in urine.

Diagnosis of type I diabetes:

1. The onset of Type 1 diabetes is typically during childhood and symptoms develop rapidly.
2. Patients with Type 1 diabetes can usually be recognized by the abrupt appearance of:
   polyuria (frequent urination),
   polydepsia (excessive thirst),
   polyphagia (excessive hunger),
3. These symptoms are usually accompanied by fatigue, weight loss, and weakness.
4. Lab investigation:
   - Fasting plasma glucose level ≥ 126 mg/dl
   - Post prandial Plasma glucose ≥ 200 mg/dl)
   - Glycated hemoglobin (HbA1C) ≥ 6.5

NB: HbA1C is the investigation of choice to monitor therapy as it gives an idea about the blood glucose level over the previous few months.



Treatment of type I diabetes:

- The treatment of choice is **exogenous insulin** injected subcutaneously to control hyperglycemia and ketoacidosis.
- Food regulation
- The blood glucose level should be monitored to avoid hypoglycemia.

Type II Diabetes

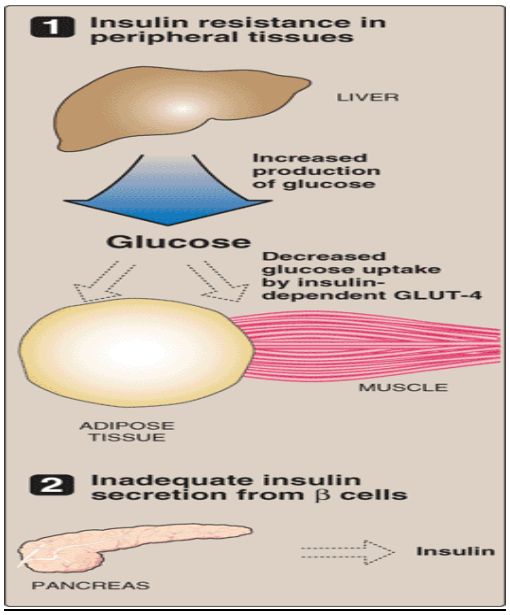
- It represents around **90%** of the diabetic population.
- Type II diabetes develops gradually and sometimes detected by routine screening.
- Patients have a combination of **insulin resistance & dysfunctional β- cells.**
- Metabolic changes are milder than type I and ketoacidosis is a rare complication**.**

Biochemical basis of Type II

- A-Insulin resistance: it is the decreased ability of target tissues e.g. adipose and muscle to respond properly to normal circulating insulin levels.
- B- Insulin resistance alone does not lead to it but a defect in β-cell function as well.

- *Dysfunctional β-cells*

- In type II diabetes, the pancreas initially retains β-cell capacity to secrete insulin.
- However, with time, the β- cells become increasingly dysfunctional and fail to secrete enough insulin to correct hyperglycemia.



Metabolic changes in type II diabetes:

It is the same as Type I except

NB: Ketosis is usually minimal or absent in type 2 patients because the presence of insulin even in the presence of insulin resistance diminishes hepatic ketogenesis.

Treatment of type II diabetes:

1. Weight reduction, exercise and diet control are often enough.
2. If not, we resort to Oral hypoglycemic drugs or even insulin in severe cases.

Complications of type II Diabetes:

1. *Hyperglycemic hyperosmolar coma:*

- Blood glucose level may reach 1000 mg/dl… severe hyperglycemia and glucosuria lead to:
  - Urinary loss of water and electrolytes
  - Osmotic diuresis
  - Severe dehydration

  Treatment
  - Restore water and electrolyte balance.
  - Injection of insulin.

2. *Hypoglycemic coma:* due to treatment overdose

Types of coma in DM:

1. Ketotic coma
2. Hyperglycemic hyperosmolar coma
3. Hypoglycemic coma

Chronic complications (effects) of diabetes (type I & II):

1- Cataract:

- In cells where entry of glucose is not dependent on insulin, elevated blood glucose leads to increased intracellular glucose and its metabolites. For example, increased intracellular sorbitol contributes to the formation of cataracts

- Glucose is reduced by aldolase reductase into sorbitol causing Osmotic damage to the cells

*NB: Insulin is not required for the entry of glucose into cells of the lens, **retina**, liver, kidney, red blood cells and in cells of the ovary and seminal vesicles.*

2- Abnormal glycation of proteins:

- Non enzymatic binding of glucoase and protein (HB, collagen of the glomerular basement membrane, proteins of small blood vessels and proteins of the nervous system)

- These glycated proteins mediate some of the early microvascular changes of diabetes

- The end products of glycation are termed **AGEs** (Advanced glycation end products).

- The **AGEs** bind to specific receptors on Endothelial cells and macrophages causing tissue damage **(Angiopathy)**

- **Angiopathy** affects small blood vessels as capillaries especially those of the kidneys and retina of the eye.

- So the long-standing elevation of blood glucose causes **diabetic retinopathy, diabetic nephropathy and diabetic neuropathy**

	Type 1 Diabetes	Type 2 Diabetes
AGE OF ONSET	Usually during childhood or puberty; symptoms develop rapidly	Frequently after age 35; symptoms develop gradually
NUTRITIONAL STATUS AT TIME OF DISEASE ONSET	Frequently undernourished	Obesity usually present
PREVALENCE	900,000 = 10% of diagnosed diabetics	10 Million = 90% of diagnosed diabetics
GENETIC PREDISPOSITION	Moderate	Very strong
DEFECT OR DEFICIENCY	β Cells are destroyed, eliminating production of insulin	Insulin resistance combined with inability of β cells to produce appropriate quantities of insulin
FREQUENCY OF KETOSIS	Common	Rare
PLASMA INSULIN	Low to absent	High early in disease; low in disease of long duration
ACUTE COMPLICATIONS	Ketoacidosis	Hyperosmolar state
TREATMENT WITH ORAL HYPOGLYCEMIC DRUGS	Unresponsive	Responsive
TREATMENT	Insulin is always necessary	Diet, exercise, oral hypoglycemic drugs; insulin may or may not be necessary